

PCT

RAW SEQUENCE LISTING DATE: 09/09/2004
PATENT APPLICATION: US/10/506,406 TIME: 15:58:04

Input Set : D:\9471-011-999.TXT

```
4 <110> APPLICANT: Swiercz, Rafal
              Selman, Steven
      5
              Jankun, Jerzy
      6
              Chorostowska-Wynimko, Joanna
      8
              Skrzypczak-Jankun, Ewa
     10 <120> TITLE OF INVENTION: MODIFIED PLASMINOGEN ACTIVATOR INHIBITOR
              TYPE-1 AND METHODS BASED THEREON
     14 <130> FILE REFERENCE: 9471-011-999
C--> 16 <140> CURRENT APPLICATION NUMBER: US/10/506,406
C--> 17 <141> CURRENT FILING DATE: 2004-09-01
     19 <150> PRIOR APPLICATION NUMBER: PCT/US03/06679
     20 <151> PRIOR FILING DATE: 2003-03-04
     22 <150> PRIOR APPLICATION NUMBER: 60/361,670
     23 <151> PRIOR FILING DATE: 2002-03-04
     25 <160> NUMBER OF SEQ ID NOS: 3
     27 <170> SOFTWARE: FastSEQ for Windows Version 4.0
     29 <210> SEQ ID NO: 1
     30 <211> LENGTH: 2876
     31 <212> TYPE: DNA
     32 <213 > ORGANISM: Hom(e) sapiens
     34 <220> FEATURE:
     35 <221> NAME/KEY: CDS
     36 <222> LOCATION: (76)...(1281)
     37 <223> OTHER INFORMATION: human PAI-1 plus 5' and 3' sequence
    39 <400> SEQUENCE: 1
     40 gaatteetge ageteageag eegeegeeag ageaggaega acegeeaate geaaggeace 60
     41 tetgagaact teagg atg cag atg tet eea gee etc ace tge eta gte etg
     42
                         Met Gln Met Ser Pro Ala Leu Thr Cys Leu Val Leu
     43
     45 ggc ctg gcc ctt gtc ttt ggt gaa ggg tct gct gtg cac cat ccc cca
                                                                           159
     46 Gly Leu Ala Leu Val Phe Gly Glu Gly Ser Ala Val His His Pro Pro
    47
                 15
                                     20
     49 tec tac gtg gec cac etg gec tea gac tte ggg gtg agg gtg ttt eag
                                                                           207
    50 Ser Tyr Val Ala His Leu Ala Ser Asp Phe Gly Val Arg Val Phe Gln
                                 35
                                                                           255
    53 cag gtg gcg cag gcc tcc aag gac cgc aac gtg gtt ttc tca ccc tat
    54 Gln Val Ala Gln Ala Ser Lys Asp Arg Asn Val Val Phe Ser Pro Tyr
                             50
                                                 55
                                                                      60
    57 ggg gtg gcc tcg gtg ttg gcc atg ctc cag ctg aca aca gga gga gaa
                                                                           303
    58 Gly Val Ala Ser Val Leu Ala Met Leu Gln Leu Thr Thr Gly Gly Glu
                         65
                                             70
    61 acc cag cag att caa gca gct atg gga ttc aag att gat gac aag
                                                                           351
    62 Thr Gln Gln Gln Ile Gln Ala Ala Met Gly Phe Lys Ile Asp Asp Lys
```

RAW SEQUENCE LISTING DATE: 09/09/2004
PATENT APPLICATION: US/10/506,406 TIME: 15:58:04

Input Set : D:\9471-011-999.TXT

										•							
63				80					85					90			
65	ggc	atg	gcc	ccc	gcc	ctc	cgg	cat	ctg	tac	aag	gag	ctc	atg	ggg	cca	399
66	Gly	Met.	Ala	Pro	Ala	Leu	Arg	His	Leu	Tyr	Lys	Glu	Leu	Met	Gly	Pro	
67			95				_	100		-	-		105		_		
69	tgg	aac	aag	gat	gag	atc	agc	acc	aca	gac	gcg	atc	ttc	gtc	cag	cgg.	447
70	Trp	Asn	Lys	Asp	Glu	Ile	Ser	Thr	Thr	Asp	Ala	Ile	Phe	Val	Gln	Arg	
71	_	110	-	_			115			_		120				_	
73	gat	ctg	aag	ctg	gtc	cag	ggc	ttc	atg	ccc	cac	ttc	ttc	agg	ctg	ttc	495
									Met								
	125		•			130	•				135					140	
77	cqq	agc	acq	qtc	aaq	caa	ata	qac	ttt	tca	qaq	ata	qaq	aqa	qcc	aqa	543
									Phe								
79	_				145			-		150					155		
81	ttc	atc	atc	aat	qac	tgg	qtq	aaq	aca	cac	aca	aaa	qqt	atq	atc	agc	591
									Thr								
83				160	-	•		-	165			-	•	170			
85	aac	ttq	ctt	aga	aaa	qqa	qcc	äta	gac	caq	ctq	aca	caa	ctq	ata	cta	639
									Asp								
87			175	•	-	•		180	-				185				
89	ata	aat	qcc	ctc	tac	ttc	aac	aac	cag	taa	aaq	act	ccc	ttc	ccc	qac	687
									Gln								
91		190			-		195	•		-	4	200				-	
93	tcc	aqc	acc	cac	cqc	cqc	ctc	ttc	cac	aaa	tca	gac	aac	aqc	act	atc	735
		_			_	_			His			_		_		_	
	205				_	210				•	215	-	•			220	
		ata	ccc	atq	atq	act	caq	acc	aac	aaq	ttc	aac	tat	act	qaq	ttc	783
				_	_	_	_		Asn	_							
99					225					230			-1-		235		
101	acc	acc	1 000	gat	ggc	cat	tac	tac	qac	ato	cta	qaa	cto	7 000	: tac	cac	831
																His	
103				240	_		-	-	245					250	_		
105	ago	gac	acc	cto	ago	ato	ttc	att	act	qee	cct	tat	: qaa	aaa	qaq	gtg	879
		_			_	_			_	-						val	
107	_	_	255					260					265	_			
109	cct	cto	: tct	. acc	cto	a'cc	aac	att	cta	aqt	acc	cac	cto	ato	: ago	cac	927
				-					_	-	-	_			_	His	
111		270					275					280					
				aac	ato	acc		cto	r ccc	cac	ctc			cto	r aac	aag	975
					_			_		_		_	_	_		Lys	,
	285	_	1			290	_			3	295					300	
			: ata	r dad	act			gac	ctc	agg			: cta	gao	aac	ctg	1023
																Leu	
119					305					310	_				315		
		ato	raco	gac			aga	cad	ttt			gac	: tto	aco		ctt	1071
		-			-		_	-		_	-	_			_	Leu	
123	_			320		- 110	9		325				- 110	330			
		gan	caa			ctc	cac	atic			ada	ato	cac			aag	1119
																. Lys	
127			335				0	340		U _11			345				
12/			555					J-# U					243				

RAW SEQUENCE LISTING DATE: 09/09/2004
PATENT APPLICATION: US/10/506,406 TIME: 15:58:04

Input Set : D:\9471-011-999.TXT

```
129 atc gag gtg aac gag agt ggc acg gtg gcc tcc tca tcc aca gct gtc
                                                                   1167
130 Ile Glu Val Asn Glu Ser Gly Thr Val Ala Ser Ser Ser Thr Ala Val
                          355
                                              360
133 ata gtc tca gcc cgc atg gcc ccc gag gag atc atc atg gac aga ccc
134 Ile Val Ser Ala Arg Met Ala Pro Glu Glu Ile Ile Met Asp Arg Pro
135 365
                       370
                                          375
137 ttc ctc ttt gtg gtc cgg cac aac ccc aca gga aca gtc ctt ttc atg
                                                                   1263
138 Phe Leu Phe Val Val Arg His Asn Pro Thr Gly Thr Val Leu Phe Met
                                      390
139
                   385
141 ggc caa gtg atg gaa ccc tgaccctggg gaaagacgcc ttcatctggg
                                                                   1311
142 Gly Gln Val Met Glu Pro
145 acaaaactgg agatgcatcg ggaaagaaga aactccgaag aaaagaattt tagtgttaat 1371 .
146 gactettet gaaggaagag aagacatttg cettttgtta aaagatggta aaccagatet 1431
147 gtctccaaga ccttggcctc tccttggagg acctttaggt caaactccct agtctccacc 1491
148 tgagaccctg ggagagaagt ttgaagcaca actcccttaa ggtctccaaa ccagacggtg 1551
149 acgcctgcgg gaccatctgg ggcacctgct tccacccgtc tctctgccca ctcgggtctg 1611
150 cagacctggt teccactgag geeetttgca ggatggaact acggggetta caggagettt 1671
151 tgtgtgcctg gtagaaacta tttctgttcc agtcacattg ccatcactct tgtactgcct 1731
152 gccaccgcgg aggaggctgg tgacaggcca aaggccagtg gaagaaacac cctttcatct 1791
153 cagagtecac tgtggcactg gccaccecte cecagtacag gggtgetgea ggtggcagag 1851
155 agtgtgcatg ggttattttg gagtgtaggt gacttgttta ctcattgaag cagatttctg 1971
156 cttcctttta tttttatagg aatagaggaa gaaatgtcag atgcgtgccc agctcttcac 2031
157 cccccaatct cttggtgggg aggggtgtac ctaaatattt atcatatcct tgcccttgag 2091
158 tgcttgttag agagaaagag aactactaag gaaaataata ttatttaaac tcgctcctag 2151
159 tgtttctttg tggtctgtgt caccgtatct caggaagtcc agccacttga ctggcacaca 2211
160 cccctccgga catccagcgt gacggagccc acactgccac cttgtggccg cctgagaccc 2271
161 tegegeeece egegeeece gegeeectet titteeecti gatggaaatt gaccatacaa 2331
162 tttcatcctc cttcagggga tcaaaaggac ggagtggggg gacagagact cagatgagga 2391
163 cagagtggtt tccaatgtgt tcaatagatt taggagcaga aatgcaaggg gctgcatgac 2451
164 ctaccaggac agaactttcc ccaattacag ggtgactcac agccgcattg gtgactcact 2511
165 tcaatgtgtc atttccggct gctgtgtgtg agcagtggac acgtgagggg ggggtgggtg 2571
166 agagagacag gcagctcgga ttcaactacc ttagataata tttctgaaaa cctaccagcc 2631
167 agagggtagg gcacaaagat ggatgtaatg cactttggga ggccaaggcg ggaggattgc 2691
168 ttgagcccag gagttcaaga ccagcctggg caacatacca agacccccgt ctctttaaaa 2751
170 attttaaaga ccaatttatg ggagaattgc acacagatgt gaaatgaatg taatctaata 2871
171 gaagc
                                                                   2876
173 <210> SEQ ID NO: 2
174 <211> LENGTH: 402
175 <212> TYPE: PRT
176 <213 > ORGANISM: Home) sapiens
178 <220> FEATURE:
179 <223> OTHER INFORMATION: human PAI-1 amino acid sequence, including signal peptide
181 <400> SEQUENCE: 2
182 Met Gln Met Ser Pro Ala Leu Thr Cys Leu Val Leu Gly Leu Ala Leu
                                      10
184 Val Phe Gly Glu Gly Ser Ala Val His His Pro Pro Ser Tyr Val Ala
```

RAW SEQUENCE LISTING DATE: 09/09/2004
PATENT APPLICATION: US/10/506,406 TIME: 15:58:04

Input Set : D:\9471-011-999.TXT

105				20					25					30		
185	ui a	T 011	. ד'ת		7 02	Dho	C1	17-1		77-1	Dho	C1 5	Cl n	Val	ת דת	Cln
	птэ	neu		261	ASP	FIIE	GIY	40	Arg	vai	FIIC	GIII	45	vai	AIA	GIII
187	71.	0	35	7 ~~	7 ~~~	7	17-1		Dha	Com	Dwo	m		3707	71-	Cor
	Ата		гуѕ	Asp	Arg	ASII		vaı	Pne	ser	PIO	60 1 y 1	GIY	Val	Ата	ser
189	**- 7	50	77-	Mak	T	a1	55	m\	mb-a	a1	a1		mh se	<u>را ۳</u>	C1 ~	C1.
		Leu	Ala	met	ьeu		ьeu	Thr	Thr	GIY	_	GIU	THE	Gln	GIII	
191		~1			16 - L	70	51	•	- 1 -	3	75	T	~ 1	W-4	77-	80
	тте	GIN	Ата	Ala		GIY	Pne	гуз	TTE	_	Asp	гуѕ	GIA	Met		Pro
193		_	_		85	_	_	~1	_	90	~ 1				95	
	Ala	Leu	Arg		Leu	Tyr	ьуѕ	GIu		Met	GIY	Pro	Trp	Asn	газ	Asp
195	~-7		_	100	_,	_			105		a 1			110		•
	GIU	тте		Thr	Tnr	Asp	Ата		Pne	vaı	GIN	Arg		Leu	гаг	Leu
197		~-3	115			_		120			-	-1	125		m)	
	Val		GLY	Phe	Met	Pro		Pne	Pne	Arg	ьeu		Arg	Ser	Thr	vai
199		130		_		_	135			· .		140	1			_
	_	GIn	Val	Asp	Pne		GIu	vai	GIU	Arg		Arg	Pne.	Ile	тте	
	145	_	-	_		150		_			155	_	_	_	_	160
	Asp	Trp	Val	Lys		His	Thr	Lys	GIY		IIe	Ser	Asn	Leu		GIY
203	_ *				165		_		_	170		_		_	175	_
	Lys	Gly	Ala		Asp	Gln	Leu	Thr	_	Leu	Val	Leu	Val	Asn	Ala	Leu
205			_	180		_	_		185	_,	_	_	_	190	_,	
	Tyr	Phe		GIÀ	GIn	Trp	Lys		Pro	Phe	Pro	Asp		Ser	Thr	His
207	_	_	195		•	_	_	200		_	_,		205		_	
	Arg	_	Leu	Phe	His	Lys		Asp	GIY	Ser	Thr		Ser	Val	Pro	Met
209		210		_,	_	_	215	_	_	_,		220	_,	1	_	_
		Ala	GIn	Thr	Asn	_	Pne	Asn	Tyr	Thr		Pne	Tnr	Thr	Pro	
	225		_	_	_	230	_	~3	_	_	235		~7		m) .	240
	GIY	His	Tyr	Tyr		тте	ьeu	GIU	ьeu		Tyr	HIS	GIY	Asp		Leu
213	~		-1		245				~ 1	250	a1	**- 7	D	•	255	77-
	ser	Met	Pne		Ата	Ата	Pro	Tyr		ьys	GIU	vai	Pro	Leu	ser	Ala
215	_		_	260				~ 3	265	-1.	~	***	M	270	a1	3
	Leu	Thr		тте	ьeu	Ser	Ата		ьeu	тте	ser	HIS		Lys	GIY	Asn
217		1	275		_	•		280	··- 7	.	5	.	285	0	.	
	мет			Leu	Pro	Arg		ьeu	vaı	Leu	Pro		Pne	Ser	ьeu	GIU
219	m1	290		3	.	3	295	D	.	~1	7	300	~1	1/- L	mla sa	7
		GIU	vai	Asp	ьeu		гуѕ	Pro	Leu	GIU		ьeu	GIY	Met	Thr	
	305	D1	3	~1	D)	310	37 -	•	D1	m1	315	T	0	7	~1	320
	мет	Pne	Arg	GIN			Ala	Asp	Pne		ser	Leu	ser	Asp		GIU
223			***	••- 7	325			.	a 3	330	*** 7	T	- 7 -	a1	335	7
	Pro	Leu	HIS		Ala	GIN	Ата	ьeu		гуѕ	vaı	ьуѕ	тте	Glu	vai	ASII
225	~ 1	.	~ 1	340	**- 7		a	0	345	m1	7 T -	**- 7	T 1.	350	0	77-
	GIU	ser	_	Thr	vaı	Ата	ser		ser	Thr	Ala	vai		Val	ser	Ala
227	•	36 - 4.	355	n	~ 1	~1	- 1 -	360	14 - L	3	3	D	365	T	Dh.	**- 7
	Arg		Ala	Pro	GIU	GIU		тте	met	Asp	Arg		Pne	Leu	Pne	vai
229		370	***		D	m1	375	m)	*** 7	.	D1	380	~ 1-	~ 1	11c 7	M
		arg	Hls	Asn	Pro		GTA	Tnr	vaı	ьeu		мес	GIY	Gln	vaı	
	385	_				390					395					400
	Glu				_											
235	<210)> SI	⊴Q II	: סמ כ	: 3		,									

RAW SEQUENCE LISTING DATE: 09/09/2004 PATENT APPLICATION: US/10/506,406 TIME: 15:58:04

Input Set : D:\9471-011-999.TXT

```
236 <211> LENGTH: 379
237 <212> TYPE: PRT
238 <213> ORGANISM: Home sapiens
240 <220> FEATURE:
241 <223> OTHER INFORMATION: human PAI-1 mature amino acid sequence
243 <400> SEQUENCE: 3
244 Val His His Pro Pro Ser Tyr Val Ala His Leu Ala Ser Asp Phe Gly
. 246 Val Arg Val Phe Gln Gln Val Ala Gln Ala Ser Lys Asp Arg Asn Val
                                   25
      20
248 Val Phe Ser Pro Tyr Gly Val Ala Ser Val Leu Ala Met Leu Gln Leu
250 Thr Thr Gly Gly Glu Thr Gln Gln Gln Ile Gln Ala Ala Met Gly Phe
252 Lys Ile Asp Asp Lys Gly Met Ala Pro Ala Leu Arg His Leu Tyr Lys
                                            75
254 Glu Leu Met Gly Pro Trp Asn Lys Asp Glu Ile Ser Thr Thr Asp Ala
                    85
                                       90
256 Ile Phe Val Gln Arg Asp Leu Lys Leu Val Gln Gly Phe Met Pro His
                                   105
               100
258 Phe Phe Arg Leu Phe Arg Ser Thr Val Lys Gln Val Asp Phe Ser Glu
259 115
                                120
260 Val Glu Arg Ala Arg Phe Ile Ile Asn Asp Trp Val Lys Thr His Thr
                         135
261 130
262 Lys Gly Met Ile Ser Asn Leu Leu Gly Lys Gly Ala Val Asp Gln Leu
                                           155
                      150
264 Thr Arg Leu Val Leu Val Asn Ala Leu Tyr Phe Asn Gly Gln Trp Lys
                                       170
                    165
266 Thr Pro Phe Pro Asp Ser Ser Thr His Arg Arg Leu Phe His Lys Ser
                                    185
268 Asp Gly Ser Thr Val Ser Val Pro Met Ala Gln Thr Asn Lys Phe
           195
                               200
270 Asn Tyr Thr Glu Phe Thr Thr Pro Asp Gly His Tyr Tyr Asp Ile Leu
                           215
272 Glu Leu Pro Tyr His Gly Asp Thr Leu Ser Met Phe Ile Ala Ala Pro
                       230
                                           235
274 Tyr Glu Lys Glu Val Pro Leu Ser Ala Leu Thr Asn Ile Leu Ser Ala
                                       250
                   245
276 Gln Leu Ile Ser His Trp Lys Gly Asn Met Thr Arg Leu Pro Arg Leu
                                   265
               260
278 Leu Val Leu Pro Lys Phe Ser Leu Glu Thr Glu Val Asp Leu Arg Lys
                               280
280 Pro Leu Glu Asn Leu Gly Met Thr Asp Met Phe Arg Gln Phe Gln Ala
                            295
                                               300
282 Asp Phe Thr Ser Leu Ser Asp Gln Glu Pro Leu His Val Ala Gln Ala
                       310
                                           315
284 Leu Gln Lys Val Lys Ile Glu Val Asn Glu Ser Gly Thr Val Ala Ser
                   325
                                       330
286 Ser Ser Thr Ala Val Ile Val Ser Ala Arg Met Ala Pro Glu Glu Ile
```

VERIFICATION SUMMARY

DATE: 09/09/2004 TIME: 15:58:05

PATENT APPLICATION: US/10/506,406

Input Set : D:\9471-011-999.TXT

Output Set: N:\CRF4\09092004\J506406.raw

L:16 M:270 C: Current Application Number differs, Replaced Current Application Number

L:17 M:271 C: Current Filing Date differs, Replaced Current Filing Date